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09/975,350	10/11/2001	Martin J. Jacobs	CP215	9510

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EXAMINER	
FUBARA, BLESSING M	
ART UNIT	PAPER NUMBER
1618	
MAIL DATE	DELIVERY MODE
04/02/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	09/975,350	JACOBS ET AL.	
	Examiner	Art Unit	
	BLESSING M. FUBARA	1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 January 2008*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,8-43,45-50,55-60 and 63-68* is/are pending in the application.

4a) Of the above claim(s) *36-43,57,58,60,64 and 65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,8-35,45-50,55,56,59,63 and 66-68* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *1/09/08*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Examiner acknowledges receipt of request for extension of time, amendment and remarks 1/09/08. Claims 41 and 42 are amended. Claims 44 and 61 are canceled. Claims 1, 3, 4, 8-43, 45-50, 55-60 and 63-68 are pending. Claims 36-43, 57, 58, 60, 64 and 65 were withdrawn from consideration and are withdrawn from consideration.

It is brought to applicant's attention that applicant has not used proper status identifiers for withdrawn claims 36-43, 57, 58, 60, 64 and 65. It is also suggested that applicant use the proper status identifiers in all future correspondences to identify all claims.

Claim Rejections - 35 USC § 102

1. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

2. Claims 1, 3, 4, 11, 14, 15, 32, 33, 45-47 and 59 remain rejected under 35 U.S.C. 102(b) as being anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over Nguyen et al. (US 5,843,347) according to the rejections on record and reiterated below.

Nguyen teaches a pharmaceutical composition comprising particles or microparticles of active ingredient, physiologically acceptable hydrophilic excipient and water (abstract). The

hydrophilic excipient comprises a polymer component and a water-soluble or water dispersible component that acts as a diluent (column 6, lines 1-5). The polymer component is selected from the group consisting of gum Arabic, xanthan gum, gum tragacanth, alginates, pectinates, polyvinylpyrrolidone, polyethylene glycols, cellulose, carboxymethyl cellulose, cellulose ethers, carboxymethyl chitin, dextran, chitosan, gelatin, acrylic and methacrylic polymers and copolymers, colloidal silica and mixtures thereof (column 6, lines 11-23). The water-soluble or water dispersible component is selected from the group consisting of lactose, glycocoll, mnnnitol, glucose, sucrose, maltodextrin, cyclodextrins and derivatives thereof (column 6, lines 44-49). The hydrophilic excipients can also comprise surfactants that are capable of oral administration and the surfactants can be polysorbates, sorbitan esters, fatty glyceride polyethers, lecithins, sodium lauryl sulfate, sodium dioctylsulfosuccinate and mixtures thereof (column 7, lines 2-7). The process of preparing the modafinil particles involves homogenization of the active ingredient in solution, suspension, or emulsion and freeze-drying or lyophilization (column 8, lines 15-24). The active ingredient is selected from the group consisting of paracetamol, probucol, piroxicam, phloroglucinol, tiadenol, flerobuterol, modafinil, dexfenfluramine, carbinoxamine maleate, loperamide, lorazepam and mixtures thereof (claim 13). Claims 45-47 recite the properties of the composition. Oral administration is route of administration and route of administration of a composition is does not patentably distinguish the claimed composition over the prior art .

The preparation is lyophilized such that the amount of water is driven to a minimum and would be less than 10%. Therefore, in the alternative, the modafinil composition of Nguyen is non-aqueous as gleaned from applicant's specification at paragraph [0020].

Response to Arguments

3. Applicant's arguments filed 1/09/08 have been fully considered but they are not persuasive.

Applicant argues that a) Nguyen's lyophilized composition cannot be a solid solution because, the Nguyen teaches at col. 2, lines 46, 50 and 53-56; col. 3, lines 1, 12 and 17-22 that the lyophilization process preserves the initial characteristics of the active ingredient as it existed in the pre-lyophilized composition and as such the modafinil will be present as discrete particles in the lyophilized product; b) because modafinil is insoluble in water, modafinil in examples 16 and 17 of Nguyen necessarily be in discrete undissolved particles in the pre-lyophilized composition and in the lyophilized product; c) compositions that contain significant quantities of particles of undissolved particles fundamentally differ from the instant compositions because those compositions are not solid solutions, applicant supports this view by citing, i) US 6,264,981 at col. 6, lines 35-39, col. 6, line 67 to col. 7, line 4, col. 8, lines 45-47 and 65-67, ii) US 5,422,384 at col. 2, lines 45-52; and iii) Sertsou et al., first full paragraph of page 100.

Response:

Claim 1 is directed to non-aqueous solution that comprises modafinil compound and at least one surfactant. The specification at paragraph [0026] of the published application defines "modafinil compound" as "modafinil, its racemic mixtures, individual isomers, acid addition salts, such as a metabolic acid of modafinil, benzhydrylsulfinylacetic acids, and its sulfone forms, hydroxylated forms, polymorphic forms, analogs, derivatives, cogeners and prodrugs

thereof." Instant claims 10-13 define what the surfactant is in the composition of claim 1. Applicant has also referred to examples 16 and 17 as containing modafinil compositions. Applicant would agree that the compositions in examples 16 and 17 contain modafinil and TWEEN 80 (also known as Polysorbate 80), which is the surfactant named in instant claims 10, 12 and 13, such the compositions disclosed in examples 16 and 17 of Nguyen after lyophilization are the same as the claimed composition recited in claims 1, 3, 10, 12 and 13, where no specific amounts of surfactant and modafinil are recited. Thus if the modafinil in claim 1 is soluble in the surfactant containing composition, then the modafinil in examples 16 and 17 would also be soluble.

Therefore, regarding a), the modafinil is in solid solution in the lyophilized product. Citation of Nguyen at col. 2, lines 46, 50 and 53-56; col. 3, lines 1, 12 and 17-22 does not negate the composition of Nguyen as meeting the composition of claim 1 because the same section that applicant relies on also refers to a number of advantages of lyophilization. One advantage is the preservation of the initial characteristics of the active ingredient; other advantages are in improving the storage stability of the active ingredients such as chemical stability, physical stability, avoidance of physical transformation of the dry products and providing of slowly dissolving substances. These advantages refers to the active agent in the dried of lyophilized product. The physical and chemical characteristics, avoidance of physical transformation of the dry product would all lead to preserving the initial characteristic of the active agent, which has to do with the biological activity of the active agent and does not maintaining the initial particles of the active agent. Regarding b) modafinil in examples 16 and 17 is the same modafinil in the claims, TWEEN 80 also known as polysorbate 80 is the same surfactant in the claims so that is

the modafinil is soluble in the claims, then modafinil would also be soluble in the examples of Nguyen. Regarding c) the prior art cited does not support applicant's arguments that the composition of Nguyen differs from the claimed composition. For example, i) US 6,264,981 at column 6, lines 35-39 talks about solid solution that is capable of being delivered via oral mucosal membrane; at column 6, line 67 to column 7, line 4, the US 6,264,981 talks about combining dissolution solvent and pharmaceutical agent to form solid solution with the pharmaceutical agent and the dissolution solvent mixing at the molecular level; and column 8, lines 45-47 and 65-67 of the US 6,264,981 describes the process of preparing solid solutions; in all these, US 6.264,981 does not provide evidence that the composition of Nguyen cannot be solid solution. ii) US 5,422,384 at column 2, lines 45-52 discusses glass/polymer composite or molecular phase glass/polymer composite that are indistinguishable at the molecular level. Lines 61 to 68 further says that "the molecular phase glass/polymer composite material solid solution of the invention has a first solute of at least one glass with a second solute of at least one polymer wherein the first solute and the second solute **are homogeneously dispersed at the molecular level**. In addition, individual chains of the first solute are chemically bonded to the individual chains of the second solute." It is also noted that a heating step is involved in the formation of the molecular phase glass/polymer composite in US 5,422,384. The claims are directed to compositions and not to process of making the composition and the composite of US 5,422,384 differs from the claimed composition so that this art relied upon by applicant does not support applicant's argument that the composition of Nguyen cannot be a solid solution. iii) the first paragraph of page 100 of Sertsou describes solid dispersion as an amorphous solid solution, describes decrease of particle size to the molecular level and wetability of the drug, and increase

in available surface area available for mass transfer. This paragraph does not support applicant's argument that the composition of Nguyen cannot be solid solution but points to amorphous solid solutions having increased surface area for mass transfer. Therefore, Nguyen teaches a composition that meets all the limitations of the claimed composition.

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

5. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 8-10, 12, 13, 16, 17-31, 34, 35, 55, 56, 63, 66 and 68 are rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al. (US 5,843,347) according to the rejections of record and as reiterated below.

Nguyen is discussed above. Regarding the amounts of surfactant in claims 8, 9, 23-25, 27-30; and regarding the amount of modafinil in claims 17 and 18, it is within the purview of the artisan to use amounts of surfactants and modafinil in the composition to provide the desired composition. However, Nguyen is silent on the optical character of the modafinil. But it is known in the art that modafinil in the absence of designation of d- or l-, is the racemic form comprises of the l- or d- form. Therefore, it would have been obvious to use the either the d- or l- or the racemic form in the preparation. In the absence of factual evidence, the use of the specific l-form of the modafinil is not inventive over the use of the racemic form.

Response to Arguments

7. Applicant's arguments filed 01/09/08 have been fully considered but they are not persuasive.

Applicant argues that d) the composition of Nguyen contains undissolved modafinil particles and there is no motivation to modify the undissolved particle compositions Nguyen to form solutions since the lyophilized microbeads are prepared form suspensions or emulsions containing undissolved particles according to col. 7, lines 2-28 and col. 8, lines 23 and 24; e) Nguyen does not direct the ordinary skilled artisan on how to make a modafinil solution given that modafinil is insoluble in water at 0.4 g/L. f)

Response:

It is brought to applicant's attention that as acknowledged by applicant, examples 16 and 17 of Nguyen describes modafinil composition/preparation that contains TWEEN 80, which is polysorbate 80 and claims 1, 3, 10, 12 and 13 are directed to compositions that contain modafinil and polysorbate 80 so that if applicant's modafinil is soluble, then the modafinil of the prior art

would be reasonably expected to be soluble. Thus regarding d), it is the examiner's position that although applicant may say that the modafinil is present as particles, it does not preclude the lyophilized product form being a solution. Secondly, although, column 7, lines 2-28 of Nguyen talks about emulsions and suspensions and particles and oil phase, it is noted that column 8, lines 23 and 24 of Nguyen contemplates preparation of a solution and the compositions in examples 16 and 17 that applicant relied on do not talk of emulsions and do not contain oils. No motivation is thus required to dissolve the particles of Nguyen because, solution is contemplated and the composition has the same surfactant as the claims. Regarding e), Nguyen directs the ordinary skilled artisan on how to prepare the composition containing modafinil as shown in examples 16 and 17 and column 8, lines 23 and 24. Modafinil in the claims is the same as the modafinil in the prior art. Both compositions contain TWEEN 80 or polysorbate 80 and thus the solubility of modafinil would be the same in either composition that contain the same surfactant.

8. Claims 47-50 and 55, 56, 67 and 68 remain rejected under 35 U.S.C. 103(a) as being unpatentable over Nguyen et al. (US 5,843,347) in view of Grebow et al. (US 5,618,845) according to the rejections of record and as reiterated below.

Nguyen is described above as containing modafinil and surfactant and solvent. Nguyen's composition is not encapsulated.

Grebow teaches a pharmaceutical composition comprising modafinil particles or modafinil pharmaceutically acceptable salt particles (abstract, column 2, column 3, lines 1-55 and claims 1 and 2) and non-toxic pharmaceutically acceptable carrier (column 4, lines 4-1%. Grebow's composition contains an appropriate dosage of between 50 mg and 700 mg of

modafinil with a preferred amount of 400 mg (column 4, lines 1 1-18 and column 10, lines 15-17). The modafinil pharmaceutical composition is administered as a tablet, capsule, powder, pill, liquid, suspension or emulsion; the modafinil composition can also be administered topically via epidermal patch or administered via direct injection (column 10, lines 18-26). Grebow further teaches a method of altering somnolent state, for example, narcolepsy, idiopathic hypersomnia and related sleep disorders by administering to a mammal a pharmaceutical composition comprising an effective amount of modafinil particles; and an effective amount of the pharmaceutical composition is defined as an amount effective for treating the somnolent state (column 3, lines 56-67). In human clinical trials, modafinil is administered to physically and mentally healthy male subjects (column 5, lines 46 to 56). Regarding claim 67, Grebow teaches liquid or suspension or emulsion composition of modafinil.

The composition of Grebow encompasses stable and unstable suspensions because the prior art does not exclude stable suspensions and thus the suspension of Grebow would be inherently stable. It is also noted that Grebow discloses suspensions containing modafinil and in the suspension modafinil is not crystalline and the particles of modafinil are suspended in the solvent. The composition of Grebow can also be administered as a liquid as described above meeting claim 67

Grebow also teaches administering the prior art composition in clinical trials to mentally and physically healthy male subjects. Orally administering modafinil particles to human subjects (column 5, lines 46-56) would necessarily bring modafinil particles in contact with the aqueous environment in the human subject since human body is mostly water. the prior art is silent on the form of the capsule. Since the prior art is silent on the form of the

capsule, hard or soft gelatin capsule, the prior art broad teaching of a capsule encompasses both soft gelatin capsule or hard capsule. The expected result would be the encapsulation of modafinil particle in soft or hard gelatin capsule meeting claims 48-50. Therefore, regarding soft or hard capsule, one of ordinary skill in the art is capable of encapsulating the composition in hard or soft in hard capsule or soft gelatin capsule. Therefore, it would have been obvious to one of ordinary skill in the art at the time the invention was made to encapsulate the solid of Nguyen in the hard or soft capsule of Grebow for administration of modafinil.

Response to Arguments

9. Applicant's arguments filed 01/09/2008 have been fully considered but they are not persuasive.

Applicant argues that f) Nguyen does not teach a solid solution because applicant disagrees that the lyophilized composition of Nguyen is a solid solution. g) Grebow does not cure that deficiency because Grebow does not teach a solid solution but teaches discrete particles of modafinil in pharmaceutical dosage forms of tablet, capsule, powder, pill, Liquid/suspension or emulsion (column 4, lines 12-18 and 18-21) and that there is mo basis to modify the composition of Grebow because doing so would represent fundamental departure form basis of the Grebow art, which is a composition comprising discrete particles of modafinil.

Response:

Grebow is relied upon for teaching the encapsulation of modafinil and it is not required to modify Grebow because it is not the primary reference. Regarding f) the examiner has provided reasoned explanation above as to why applicant's arguments are not persuasive that the

composition of Nguyen is not a solid solution because the references provided by applicant to support applicant's position do not prove that the product of Nguyen is not a solid solution. Regarding g) Grebow was relied upon to show that modafinil composition in liquid or emulsion form can be encapsulated so that the ordinary skilled artisan would have reasonable expectation of success to encapsulate the product of Nguyen for oral administration. Modification of Grebow is not required because, Grebow is a not the primary reference and encapsulation of the product of Nguyen does not lead to dissolution of the particles of Grebow.

Claim 1 is a non-aqueous composition comprising modafinil compound and at least one surfactant with the composition having the characteristic that it would form an aqueous, liquid, homogeneous, stable composition of non-crystalline particles when contacted with an aqueous medium. The composition of Nguyen is a non aqueous solution comprising modafinil and surfactant and would inherently have the characteristic that when it is contacted with aqueous medium it would inherently form aqueous, liquid, homogeneous, stable composition of non-crystalline particles.

No claim is allowed.

10. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to BLESSING M. FUBARA whose telephone number is (571)272-0594. The examiner can normally be reached on 7 a.m. to 5:30 p.m. (Monday to Thursday).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael G. Hartley can be reached on (571) 272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

/Michael G. Hartley/
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